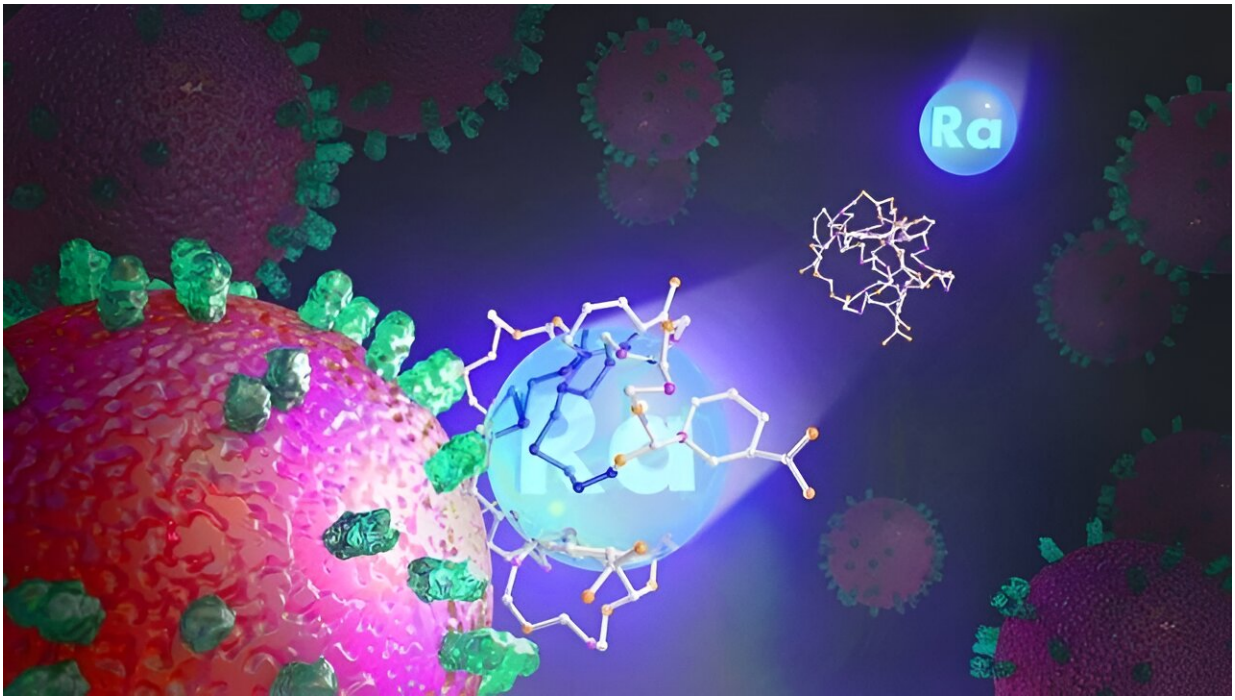
Capturing the chemistry of radium-223 for cancer treatment

September 7 2023



This image depicts a binding molecule delivering radium-223 to a cancer cell. Credit: Adam Malin, Oak Ridge National Laboratory

Scientists need a better understanding of the chemistry of radium to be able to target the isotope radium-223 (Ra-223) to cancer cells. Once delivered, Ra-223 can destroy those cells with alpha particles, a type of radiation.

In a 2022 study published in *Chemical Communications*, researchers investigated radium's chemistry by looking at how it interacts with two chelators, or binding molecules, called macropa and DOTA. Doctors use both chelators in targeted alpha cancer therapy. Through experiments and computer-driven models, the researchers discovered that macropa is the strongest chelator for binding radium identified so far. They also gained information about how the structure and properties of these chelators affect how well they bind to radium.

Until now, there have been few efforts to get information on how radium binds with known chelators. To address this gap, scientists at Oak Ridge National Laboratory (ORNL) used experiments and computer-driven models to learn about two state-of-the-art binding molecules, macropa and DOTA. Researchers already knew these two molecules could bind the radium ion in water, but they didn't know how stable those bonds were. Past studies looked at only simple organic molecules that are less relevant for use in medicine.

The work determined that the Ra–macropa complex had a more stable bond than that of any other studied Ra complexes under normal biological conditions. The Ra–DOTA complex was only moderately stable when the sodium ion was present, but its stability increased under sodium-free conditions. The study showed that, as scientists already had thought, chelators form bonds with radium that are primarily ionic. That means highly charged chelators can form highly stable complexes.

But the study also highlighted how important it is to look at the effects of sodium and other competing ions present in the body when finding the right chelators for Ra-223-based targeted alpha therapy. Scientists must consider ionic interactions, metal-ion selectivity and the chemical makeup of the chelator when designing molecules to stabilize radium.

Ra-223 has already been approved by the Food and Drug Administration

for treating prostate cancer patients whose cancer has spread to the bone. This research is significant as it means Ra-223 could also treat cancers outside the bone. It gives information about the specific kind of chelators needed to successfully bind this radioactive ion to a molecule that can deliver it directly to cancer in the body.

This new knowledge about radium's properties will help researchers find the best possible chelator to bind Ra-223 and expand its use in cancer therapy. Ra-223 is available from the DOE Isotope Program's National Isotope Development Center.

More information: Alexander S. Ivanov et al, Elucidating the coordination chemistry of the radium ion for targeted alpha therapy, *Chemical Communications* (2022). DOI: 10.1039/D2CC03156F

Provided by US Department of Energy